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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,064	06/25/2001	James M. Anderson	OCR-754.cip	9892

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Carmody & Torrance LLP
50 Leavenworth Street
PO Box1110
Waterbury, CT 06721-1110

EXAMINER	
NOLAN, PATRICK J	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,064	ANDERSON ET AL.	
	Examiner	Art Unit	
	Patrick J. Nolan	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

1. Claims 1-3 and 27-32 are pending.

2. Applicant's amendment submitted 3-9-05 has been entered.

3. Upon the entry of said amendment, the Finality of the last office action is removed. A new Non-Final office action is set forth below.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of a polypeptide that is 60%, 80% or 90% identical to residues 33-522 or 89-138 or 196-246 SEQ ID NO. 2. The claims are drawn to a genus of polypeptides that are not sufficiently described. Applicant has disclosed one polypeptide sequence and three fragments 100% derived from SEQ ID NO. 2. The specification fails to describe these genus polypeptide sequences. The full scope in Applicant's invention encompasses making any one of 20 changes to any one of 490 amino acids (60% homology would allow one to change any one of up to 208 amino acids in a 522 amino acid fragment by any of the known 20 amino acids). The full scope of Applicant's claimed invention is 2.3×10^{46} polypeptides. Does Applicant contend that the written description of one sequence describes a genus of 2.3×10^{46} polypeptides, just because they have claimed the sequence? The Examiner disagrees. In The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) the Court recognized that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the

description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus.

See the Written description guidelines from the Federal Register Vol. 66, No. 4, Friday January 5, 2001

For each claim drawn to a genus:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A ''representative number of species'' means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. What constitutes a ''representative number'' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a ''representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 USC 112 1st paragraph.

Applicant's arguments filed 6-23-03 have been fully considered but are not found persuasive.

Applicant argues the recitation of one species, with the recited functional limitation and an assay for determining which percent homologues posses that activity is adequate written description for claimed genus. Applicant further argues the current claimed invention complies with the analysis provided by Example 14, product by Function, Synopsis of Application of Written Description Guidelines, pp. 53-55.

However, the significant difference between the currently claimed invention and the example provided in the Guidelines, is the scope of the claims. In the example there was no substantial variation, because the claims presented needed to have both catalytic activity and have 95% identity to the claimed sequence. While the functional recitation is sufficient, the difference in the scope of a claim for peptide that 60% homologous versus one that has 95% identity is massive. As such there is substantial variation between the disclosed specie and the recited genus.

6. Claims 1-3 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the exact fragment sequences, does not reasonably provide enablement for fragment that are homologous to the SEQ ID NOS for being able to inhibit the barrier properties of epithelial or endothelial cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention requires the fragments to be able to inhibit the barrier properties of epithelial or endothelial cells. In a review of the specification, it is clear Applicant has only working examples of two fragments derived 100% from SEQ ID NO. 2 that can perform this function. The full scope in Applicant's invention encompasses making any one of 20 changes to any one of 490 amino acids (60% homology would allow one to change any one of up to 208 amino acids in a 522 amino acid fragment by any of the known 20 amino acids). The full scope of Applicant's claimed invention is 2.3×10^{46} polypeptides. There is no guidance as to which amino acids should be changed, nor what should they be changed to in order to preserve the functional limitation of being able to inhibit the barrier properties of epithelial or endothelial

cells. The state of the art in protein function prediction Skolnick et al (U) teaches that sequence based methods for function prediction are inadequate because of the multifunctional nature of proteins (see abstract, in particular). Skolnick et al further teaches that just knowing the structure is also insufficient for prediction of multiple functional sites. Further, "inaccurate use of the sequence-to-function methods has led to significant function-annotation errors in the sequence databases," i.e., use of the method perpetuates larger and larger errors. In addition Ngo et al., (V), newly cited, in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) teaches the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see, it would require an undue amount of experimentation for one of skill in the art to arrive at the other 2.3 X 10^{46} amino acid peptides that have the ability to inhibit the barrier properties of epithelial or endothelial cells. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain barrier inhibitory activity, and the fact that the specification has no working examples demonstrating any sequence homologues performing the required functional limitation, it would be unpredictable and require an undue amount of experimentation to practice the full scope of Applicant's claimed invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has no support in the originally filed specification or claims for a fragment that is 60% homologous to residues 33-522 of SEQ ID NO. 2.

8. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is 571-272-0847.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571-272-0841.

Patrick J. Nolan, Ph.D.
Primary Examiner, Group 1640
June 6, 2005